

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Currently Amended) A strain of *M. bovis* BCG or *M. microti*, wherein said strain has integrated all or part of the DNA fragment, ~~named~~ RD1-2F9, ~~of which~~ comprises 31808 pb of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), ~~as shown in~~ and which is designated as SEQ ID No 1, and which is responsible for enhanced immunogenicity and increased persistence of BCG to the tubercle bacilli.

2. (Canceled) A strain of *M. bovis* BCG or *M. microti* according to claim 1, wherein said strain has integrated all or part of the fragment of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*) as shown in SEQ ID No 2 responsible for enhanced immunogenicity and increased persistence of BCG to the tubercle bacilli.

Please ask the inventors to confirm that SEQ ID NO. 2 is equivalent to RD1.

3. (Canceled)

4. (Currently Amended) A strain according to claim 1, ~~which~~ wherein said strain has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), ~~which~~ wherein the integrated DNA comprises at least ~~one, two, three~~ seven or more ~~gene(s)~~ genes or fragments thereof selected from the group consisting of

Rv3861 (SEQ ID No 4), Rv3862 (SEQ ID No 5), Rv3863 (SEQ ID No 6), Rv3864 (SEQ ID No 7), Rv3865 (SEQ ID No 8), Rv3866 (SEQ ID No 9), Rv3867 (SEQ ID No 10), Rv3868 (SEQ ID No 11), Rv3869 (SEQ ID No 12), Rv3870 (SEQ ID No 13), Rv3871 (SEQ ID No 14), Rv3872 (SEQ ID No 15, mycobacterial PE), Rv3873 (SEQ ID No 16, PPE), Rv3874 (SEQ ID No 17, CFP-10), Rv3875 (SEQ ID No 18, ESAT-6), Rv3876 (SEQ ID No 19), Rv3877 (SEQ ID No 20), Rv3878 (SEQ ID No 21), Rv3879 (SEQ ID No 22), Rv3880 (SEQ ID No 23), Rv3881 (SEQ ID No 24), Rv3882 (SEQ ID No 25), Rv3883 (SEQ ID No 26), Rv3884 (SEQ ID No 27), and Rv3885 (SEQ ID No 28).

5. (Currently Amended) A strain according to claim 1, ~~which~~ wherein said strain has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), ~~which~~ wherein the integrated DNA comprises at least one, ~~two, three or more gene(s)~~ gene or fragment thereof selected from the group consisting of: Rv3867 (SEQ ID No 10), Rv3868 (SEQ ID No 11), Rv3869 (SEQ ID No 12), and Rv3870 (SEQ ID No 13), combined with at least one gene or fragment thereof selected from the group consisting of: Rv3871 (SEQ ID No 14), Rv3872 (SEQ ID No 15, mycobacterial PE), Rv3873 (SEQ ID No 16, PPE), Rv3874 (SEQ ID No 17, CFP-10), Rv3875 (SEQ ID No 18, ESAT-6), Rv3876 (SEQ ID No 19), and Rv3877 (SEQ ID No 20).

6. (Canceled)

7. (Currently Amended) A strain according to claim 1, ~~which~~ wherein said strain has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or

any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), ~~which~~ wherein the integrated DNA comprises at least ~~four~~ seven genes or fragments thereof selected from the group consisting of Rv3861 (SEQ ID No 4), Rv3862 (SEQ ID No 5), Rv3863 (SEQ ID No 6), Rv3864 (SEQ ID No 7), Rv3865 (SEQ ID No 8), Rv3866 (SEQ ID No 9), Rv3867 (SEQ ID No 10), Rv3868 (SEQ ID No 11), Rv3869 (SEQ ID No 12), Rv3870 (SEQ ID No 13), Rv3871 (SEQ ID No 14), Rv3872 (SEQ ID No 15, mycobacterial PE), Rv3873 (SEQ ID No 16, PPE), Rv3874 (SEQ ID No 17, CFP-10), Rv3875 (SEQ ID No 18, ESAT-6), Rv3876 (SEQ ID No 19), Rv3877 (SEQ ID No 20), Rv3878 (SEQ ID No 21), Rv3879 (SEQ ID No 22), Rv3880 (SEQ ID No 23), Rv3881 (SEQ ID No 24), Rv3882 (SEQ ID No 25), Rv3883 (SEQ ID No 26), Rv3884 (SEQ ID No 27),₁ and Rv3885 (SEQ ID No 28), provided that it comprises Rv3874 (SEQ ID No 17, CFP-10) and/or Rv3875 (SEQ ID No 18, ESAT-6).

8. (Canceled)

9. (Currently Amended) A strain according to claim 1, ~~which~~ wherein said strain has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), ~~which~~ wherein the integrated DNA comprises at least Rv3871 (SEQ ID No 14), Rv3875 (SEQ ID No 18, ESAT-6),₁ and Rv3877 (SEQ ID No 20).

10. (Currently Amended) A strain according to claim 1, ~~which~~ wherein said strain has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), ~~which~~ wherein the integrated DNA comprises at least Rv3871 (SEQ

ID No 14), Rv3875 (SEQ ID No 18, ESAT-6), Rv3876 (SEQ ID No 19) and Rv3877 (SEQ ID No 20).

11. (Currently Amended) A strain according to ~~one of claims 8 to 10~~ which claim 10, wherein said strain has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), which further comprises Rv3874 (SEQ ID No 17, CFP-10).

12. (Currently Amended) A strain according to ~~one of claims 8 to 11~~ which claim 11, wherein said strain has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), ~~which~~ wherein the integrated DNA further comprises Rv3872 (SEQ ID No 15, mycobacterial PE).

13. (Currently Amended) A strain according to ~~one of claims 8 to 12~~ which claim 12, wherein said strain has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), ~~which~~ wherein the integrated DNA further comprises Rv3873 (SEQ ID No 16, PPE).

14. (Currently Amended) A strain according to ~~one of claims 8 to 13~~ which claim 13, wherein said strain has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), ~~which~~ wherein the integrated DNA further comprises at least one, ~~two, three or four gene(s)~~ gene selected from Rv3861 (SEQ ID

No 4), Rv3862 (SEQ ID No 5), Rv3863 (SEQ ID No 6), Rv3864 (SEQ ID No 7), Rv3865 (SEQ ID No 8), Rv3866 (SEQ ID No 9), Rv3867 (SEQ ID No 10), Rv3868 (SEQ ID No 11), Rv3869 (SEQ ID No 12), Rv3870 (SEQ ID No 13), Rv3878 (SEQ ID No 21), Rv3879 (SEQ ID No 22), Rv3880 (SEQ ID No 23), Rv3881 (SEQ ID No 24), Rv3882 (SEQ ID No 25), Rv3883 (SEQ ID No 26), Rv3884 (SEQ ID No 27), and Rv3885 (SEQ ID No 28).

15. (Canceled)

16. (Canceled)

17. (Canceled)

18. (Currently Amended) A strain according to ~~one of claims 4 to 17~~ claim 1, wherein the coding sequence of the integrated gene is in frame with its natural promoter or with an exogenous promoter, such as a promoter capable of directing high level of expression of said coding sequence.

19. (Currently Amended) A strain according to ~~one of claims 4 to 17~~ claim 1, wherein the said integrated gene is mutated so as to maintain the improved immunogenicity while decreasing the virulence of the strain.

20. (Currently Amended) A strain according to claim 18 ~~or 19~~, wherein said strain only carries parts of the genes coding for ESAT-6 or CFP-10 in a mycobacterial expression vector under the control of a promoter, more particularly an hsp60 promoter.

21. (Previously Presented) A strain according to claim 18, wherein said strain carries at least one portion of the esat-6 gene that codes for immunogenic 20-mer peptides of ESAT-6 active as T-cell epitopes.

22. (Previously Presented) A strain according to claim 19, wherein the *esat-6* encoding gene is altered by directed mutagenesis in a way that most of the immunogenic peptides of ESAT-6 remain intact, but the biological functionality of ESAT-6 is lost.

23. (Previously Presented) A strain according to claim 19, wherein the *CFP-10* encoding gene is altered by directed mutagenesis in a way that most of the immunogenic peptides of CFP-10 remain intact, but the biological functionality of CFP-10 is lost.

24. (Currently Amended) *M. bovis* BCG::RD1 strains, which have integrated a cosmid herein referred to as either RD1-2F9 and or RD1-AP34, which are contained in the *E. coli* strains deposited at the CNCM under the accession number I-2831 and I-2832 respectively.

25. (Currently Amended) *M. bovis* BCG::RD1 strain, which has integrated the insert of the cosmid RD1-AP34, said cosmid corresponding ~~which corresponds~~ to the 3909 bp fragment of the *M. tuberculosis* H37Rv genome from region 4350459 bp to 4354367 bp cloned, as shown in SEQ ID No 3.

26. (Currently Amended) *M. bovis* BCG::RD1 strain, which has integrated the insert of the cosmid RD1-2F9 (~ 32 kb), said cosmid corresponding to ~~that covers~~ the region of the *M. tuberculosis* genome AL123456 from ca. 4337 kb to ca. 4369 kb, as shown in SEQ ID No 1.

27. (Withdrawn) *M. microti*::RD1 strain which has integrated the insert of the cosmid RD1-AP34 which corresponds to the 3909 bp fragment of the *M. tuberculosis*

H37Rv genome from region 4350459 bp to 4354367 bp cloned as shown in SEQ ID No 3).

28. (Withdrawn) *M. microti*::RD1 strain which has integrated the insert of the cosmid RD1-2F9 (~ 32 kb) that covers the region of the *M. tuberculosis* genome AL123456 from ca 4337 kb to ca. 4369 kb as shown in SEQ ID No 1.

29. (Currently Amended) A method for preparing and selecting improved *M. bovis* BCG or *M. microti* strains defined in ~~any one of claims 1 to 28~~ claim 1, comprising a step consisting of modifying said strains by insertion, deletion, or mutation in the integrated portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), more particularly in the *esat-6* or *CFP-10* gene, said method leading to strains that are less virulent for immuno-depressed individuals.

30. (Withdrawn) A cosmid or a plasmid comprising a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), said portion of DNA comprising at least one, two, three or more gene(s) selected from Rv3861 (SEQ ID No 4), Rv3862 (SEQ ID No 5), Rv3863 (SEQ ID No 6), Rv3864 (SEQ ID No 7), Rv3865 (SEQ ID No 8), Rv3866 (SEQ ID No 9), Rv3867 (SEQ ID No 10), Rv3868 (SEQ ID No 11), Rv3869 (SEQ ID No 12), Rv3870 (SEQ ID No 13), Rv3871 (SEQ ID No 14), Rv3872 (SEQ ID No 15, mycobacterial PE), Rv3873 (SEQ ID No 16, PPE), Rv3874 (SEQ ID No 17, CFP-10), Rv3875 (SEQ ID No 18, ESAT-6), Rv3876 (SEQ ID No 19), Rv3877 (SEQ ID No 20), Rv3878 (SEQ ID No 21), Rv3879 (SEQ ID No 22), Rv3880

(SEQ ID No 23), Rv3881 (SEQ ID No 24), Rv3882 (SEQ ID No 25), Rv3883 (SEQ ID No 26), Rv3884 (SEQ ID No 27) and Rv3885 (SEQ ID No 28).

31. (Withdrawn) A cosmid or a plasmid comprising a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), said portion of DNA comprising at least one, two, three or more gene(s) selected from Rv3867 (SEQ ID No 10), Rv3868 (SEQ ID No 11), Rv3869 (SEQ ID No 12), Rv3870 (SEQ ID No 13), Rv3871 (SEQ ID No 14), Rv3872 (SEQ ID No 15, mycobacterial PE), Rv3873 (SEQ ID No 16, PPE), Rv3874 (SEQ ID No 17, CFP-10), Rv3875 (SEQ ID No 18, ESAT-6), Rv3876 (SEQ ID No 19) and Rv3877 (SEQ ID No 20).

32. (Withdrawn) A cosmid or a plasmid comprising a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), said portion of DNA comprising at least one gene selected from Rv3871 (SEQ ID No 14), Rv3872 (SEQ ID No 15, mycobacterial PE), Rv3873 (SEQ ID No 16, PPE), Rv3874 (SEQ ID No 17, CFP-10), Rv3875 (SEQ ID No 18, ESAT-6) and Rv3876 (SEQ ID No 12).

33. (Withdrawn) A cosmid or a plasmid according to any of claims 30 to 32 comprising Rv3874 encoding CFP-10, Rv3875 encoding ESAT-6 or both or a part of them.

34. (Withdrawn) A cosmid or a plasmid according to any of claims 30 to 33 comprising a mutated gene selected among Rv3861 to Rv3885.

35. (Withdrawn) A cosmid or a plasmid according to claim 30 which comprises at least four genes selected from Rv3861 (SEQ ID No 4), Rv3862 (SEQ ID No 5), Rv3863 (SEQ ID No 6), Rv3864 (SEQ ID No 7), Rv3865 (SEQ ID No 8), Rv3866 (SEQ ID No 9), Rv3867 (SEQ ID No 10), Rv3868 (SEQ ID No 11), Rv3869 (SEQ ID No 12), Rv3870 (SEQ ID No 13), Rv3871 (SEQ ID No 14), Rv3872 (SEQ ID No 15, mycobacterial PE), Rv3873 (SEQ ID No 16, PPE), Rv3874 (SEQ ID No 17, CFP-10), Rv3875 (SEQ ID No 18, ESAT-6), Rv3876 (SEQ ID No 19), Rv3877 (SEQ ID No 20), Rv3878 (SEQ ID No 21), Rv3879 (SEQ ID No 22), Rv3880 (SEQ ID No 23), Rv3881 (SEQ ID No 24), Rv3882 (SEQ ID No 25), Rv3883 (SEQ ID No 26), Rv3884 (SEQ ID No 27) and Rv3885 (SEQ ID No 28), provided that it comprises Rv3874 (SEQ ID No 17, CFP-10) and/or Rv3875 (SEQ ID No 18, ESAT-6)).

36. (Withdrawn) A cosmid or a plasmid according to claim 30 which comprises at least Rv3871 (SEQ ID No 14), Rv3875 (SEQ ID No 18, ESAT-6) and Rv3876 (SEQ ID No 19)).

37. (Withdrawn) A cosmid or a plasmid according to claim 30 which comprises at least Rv3871 (SEQ ID No 14), Rv3875 (SEQ ID No 18, ESAT-6) and Rv3877 (SEQ ID No 20).

38. (Withdrawn) A cosmid or a plasmid according to claim 30 comprising at least Rv3871 (SEQ ID No 14), Rv3875 (SEQ ID No 18, ESAT-6), Rv3876 (SEQ ID No 19) and Rv3877 (SEQ ID No 20).

39. (Withdrawn) A cosmid or a plasmid according to one of claims 36 to 38 which further comprises Rv3872 (SEQ ID No 15, mycobacterial PE) Rv3873 (SEQ ID No 16, PPE) Rv3874 (SEQ ID No 17, CFP-10).

40. (Withdrawn) A cosmid or a plasmid according to one of claims 36 to 38 which further comprises at least one, two, three or four gene(s) selected from Rv3861 (SEQ ID No 4), Rv3862 (SEQ ID No 5), Rv3863 (SEQ ID No 6), Rv3864 (SEQ ID No 7), Rv3865 (SEQ ID No 8), Rv3866 (SEQ ID No 9), Rv3867 (SEQ ID No 10), Rv3868 (SEQ ID No 11), Rv3869 (SEQ ID No 12), Rv3870 (SEQ ID No 13), Rv3878 (SEQ ID No 21), Rv3879 (SEQ ID No 22), Rv3880 (SEQ ID No 23), Rv3881 (SEQ ID No 24), Rv3882 (SEQ ID No 25), Rv3883 (SEQ ID No 26), Rv3884 (SEQ ID No 27) and Rv3885 (SEQ ID No 28).

41. (Withdrawn) A cosmid herein referred as RD1-2F9 and RD1-AP34 contained in the *E. coli* strains deposited at the CNCM under the accession number I-2831 and I-2832 respectively.

42. (Withdrawn) Use of a cosmid or a plasmid according to one of claims 30 to 41 for transforming *M. bovis* BCG or *M. microti*.

43. (Currently Amended) A pharmaceutical composition comprising a strain according to ~~one of claims 1 to 27~~ claim 1 and a pharmaceutically acceptable carrier.

44. (Withdrawn) A pharmaceutical composition according to claim 40 containing suitable pharmaceutically-acceptable carriers comprising excipients and auxiliaries which facilitate processing of the living vaccine into preparations which can be used pharmaceutically.

45. (Withdrawn) A pharmaceutical composition according to claim 40 or 41 which is suitable for intravenous or subcutaneous administration.

46. (Currently Amended) A vaccine comprising a strain according to ~~one of claims 1 to 28~~ claim 1 and a suitable carrier.

47. (Currently Amended) A product comprising a strain according to ~~one of claims 1 to 28~~ claim 1 and at least one protein selected from ESAT-6 and CFP-10, or epitope derived thereof for a separate, simultaneous, or sequential use for treating tuberculosis.

48. (Currently Amended) The use of a strain according to ~~one of claims 1 to 28~~ claim 1 for preparing a medicament or a vaccine for preventing or treating tuberculosis.

49. (Currently Amended) The use of a strain according to ~~one of claims 1 to 28~~ claim 1 as an adjuvant/immunomodulator for preparing a medicament for the treatment of superficial bladder cancer.

50. (Withdrawn) A method for the identification at the species level of members of the *M. tuberculosis* complex by means of markers for RD1^{mic} and RD5^{mic} as molecular diagnostic test.

51. (Withdrawn) A method according to claim 50 comprising the use of a primer selected from:

primer esat-6F GTCACGTCCATTCATTCCCT (SEQ ID No 32),

primer esat-6R ATCCCAGTGACGTTGCCTT (SEQ ID No 33),

primer RD1^{mic} flanking region F GCAGTGCAAAGGTGCAGATA (SEQ ID No 34),

primer RD1^{mic} flanking region R GATTGAGACACTTGCCACGA (SEQ ID No 35),
primer RD5^{mic} flanking region F GAATGCCGACGTCATATCG (SEQ ID No 39),
primer RD5^{mic} flanking region R CGGCCACTGAGTTCGATTAT (SEQ ID No 40)
and the complementary sequences of said primers.

52. (Withdrawn) A diagnostic kit for the identification at the species level of members of the *M. tuberculosis* complex comprising DNA probes and primers specifically hybridizing to a DNA portion of the RD1 or RD5 region of *M. tuberculosis*, more particularly probes hybridizing under stringent conditions to a gene selected from Rv3871 (SEQ ID No 14), Rv3872 (SEQ ID No 15, mycobacterial PE), Rv3873 (SEQ ID No 16, PPE), Rv3874 (SEQ ID No 17, CFP-10), Rv3875 (SEQ ID No 18, ESAT-6), Rv3876 (SEQ ID No 19) and Rv3877 (SEQ ID No 20), preferably CFP-10 and ESAT-6.

53. (Withdrawn) A diagnostic kit according to claim 52 comprising a probe or primer selected from :

primer esat-6F GTCACGTCCATTCATTCCCT (SEQ ID No 32),
primer esat-6R ATCCCAGTGACGTTGCCTT) (SEQ ID No 33),
primer RD1^{mic} flanking region F GCAGTGCAAAGGTGCAGATA (SEQ ID No 34),
primer RD1^{mic} flanking region R GATTGAGACACTTGCCACGA (SEQ ID No 35),
primer RD5^{mic} flanking region F GAATGCCGACGTCATATCG (SEQ ID No 39),
primer RD5^{mic} flanking region R CGGCCACTGAGTTCGATTAT (SEQ ID No 40)
and the complementary sequences of said primers.

54. (Withdrawn) A diagnostic kit for the identification at the species level of members of the *M. tuberculosis* complex comprising at least one, two, three or more antibodies directed to mycobacterial PE, PPE, CFP-10, ESAT-6.

55. (Withdrawn) A diagnostic kit according to claim 54 wherein it comprises antibodies directed to CFP-10 and ESAT-6.

56. (Withdrawn) Virulence markers associated with RD1 and/or RD5 regions of the genome of *M. tuberculosis* or a part of these regions.

57. (Currently Amended) The use of a strain according to ~~one of claims 1 to 28~~ claim 1 as a carrier for the expression of a molecule or an heterologous antigen that are of therapeutic or prophylactic interest.

58. (Withdrawn) A purified nucleic acid corresponding to the *Mycobacterium* DNA inserted in a cosmid according to any of claims 30 to 41.

59. (Withdrawn) The purified nucleic acid according to claim 58 which corresponds to the insert of cosmid RD1-2F9 or cosmid RD1-AP34.

60. (New) A strain according to claim 1, wherein the strain has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), wherein the integrated DNA comprises at least one gene or fragment thereof selected from the group consisting of Rv3861 (SEQ ID No 4), Rv3862 (SEQ ID No 5), Rv3863 (SEQ ID No 6), Rv3864 (SEQ ID No 7), Rv3865 (SEQ ID No 8), Rv3866 (SEQ ID No 9), Rv3867 (SEQ ID No 10), Rv3868 (SEQ ID No 11), Rv3869 (SEQ ID No 12), Rv3870 (SEQ ID No 13), Rv3877 (SEQ ID No 20), Rv3878 (SEQ ID No 21), Rv3879 (SEQ ID No 22),

Rv3880 (SEQ ID No 23), Rv3881 (SEQ ID No 24), Rv3882 (SEQ ID No 25), Rv3883 (SEQ ID No 26), Rv3884 (SEQ ID No 27) and Rv3885 (SEQ ID No 28) in combination with at least one gene or fragment thereof selected from the group consisting of Rv3871 (SEQ ID No 14), Rv3872 (SEQ ID No 15, mycobacterial PE), Rv3873 (SEQ ID No 16, PPE), Rv3874 (SEQ ID No 17, CFP-10), Rv3875 (SEQ ID No 18, ESAT-6), Rv3876 (SEQ ID No 19).

61. (New) A strain according to claim 1, wherein the strain has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), wherein the integrated DNA comprises at least one gene or fragment thereof selected from the group consisting of Rv3861 (SEQ ID No 4), Rv3862 (SEQ ID No 5), Rv3863 (SEQ ID No 6), Rv3864 (SEQ ID No 7), Rv3865 (SEQ ID No 8), Rv3866 (SEQ ID No 9), Rv3867 (SEQ ID No 10), Rv3868 (SEQ ID No 11), Rv3869 (SEQ ID No 12), Rv3870 (SEQ ID No 13) in combination with at least one gene or fragment thereof selected from the group consisting of Rv3871 (SEQ ID No 14), Rv3872 (SEQ ID No 15, mycobacterial PE), Rv3873 (SEQ ID No 16, PPE), Rv3874 (SEQ ID No 17, CFP-10), Rv3875 (SEQ ID No 18, ESAT-6), Rv3876 (SEQ ID No 19).

62. (New) A strain according to claim 1, which has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), wherein the integrated DNA comprises at least one gene or fragment thereof selected from the group consisting of Rv3877 (SEQ ID No 20), Rv3878 (SEQ ID No 21), Rv3879 (SEQ ID

No 22), Rv3880 (SEQ ID No 23), Rv3881 (SEQ ID No 24), Rv3882 (SEQ ID No 25), Rv3883 (SEQ ID No 26), Rv3884 (SEQ ID No 27) and Rv3885 (SEQ ID No 28) in combination with at least one gene or fragment thereof selected from the group consisting of Rv3871 (SEQ ID No 14), Rv3872 (SEQ ID No 15, mycobacterial PE), Rv3873 (SEQ ID No 16, PPE), Rv3874 (SEQ ID No 17, CFP-10), Rv3875 (SEQ ID No 18, ESAT-6), Rv3876 (SEQ ID No 19).

63. (New) A strain according to claim 1, wherein the strain has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), wherein the integrated DNA comprises at least one gene or fragment thereof selected from the group consisting of Rv3861 (SEQ ID No 4), Rv3862 (SEQ ID No 5), Rv3863 (SEQ ID No 6), Rv3864 (SEQ ID No 7), Rv3865 (SEQ ID No 8), Rv3866 (SEQ ID No 9), Rv3867 (SEQ ID No 10), Rv3868 (SEQ ID No 11), Rv3869 (SEQ ID No 12), Rv3870 (SEQ ID No 13), , Rv3877 (SEQ ID No 20), Rv3878 (SEQ ID No 21), Rv3879 (SEQ ID No 22), Rv3880 (SEQ ID No 23), Rv3881 (SEQ ID No 24), Rv3882 (SEQ ID No 25), Rv3883 (SEQ ID No 26), Rv3884 (SEQ ID No 27) and Rv3885 (SEQ ID No 28) in combination with at least one gene or fragment thereof selected from the group consisting of Rv3871 (SEQ ID No 14), Rv3872 (SEQ ID No 15, mycobacterial PE), Rv3873 (SEQ ID No 16, PPE), Rv3874 (SEQ ID No 17, CFP-10), Rv3875 (SEQ ID No 18, ESAT-6), Rv3876 (SEQ ID No 19), provided that it comprises Rv3874 (SEQ ID No 17, CFP-10) and/or Rv3875 (SEQ ID No 18, ESAT-6).

64. (New) A strain according to claim 1, wherein the strain has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), wherein the integrated DNA comprises at least one gene or fragment thereof selected from the group consisting of Rv3861 (SEQ ID No 4), Rv3862 (SEQ ID No 5), Rv3863 (SEQ ID No 6), Rv3864 (SEQ ID No 7), Rv3865 (SEQ ID No 8), Rv3866 (SEQ ID No 9), Rv3867 (SEQ ID No 10), Rv3868 (SEQ ID No 11), Rv3869 (SEQ ID No 12), Rv3870 (SEQ ID No 13), Rv3880 (SEQ ID No 23), Rv3881 (SEQ ID No 24), Rv3882 (SEQ ID No 25), Rv3883 (SEQ ID No 26), Rv3884 (SEQ ID No 27), or Rv3885 (SEQ ID No 28) in combination with at least one gene or fragment thereof selected from the group consisting of Rv3871 (SEQ ID No 14), Rv3872 (SEQ ID No 15, mycobacterial PE), Rv3873 (SEQ ID No 16, PPE), Rv3874 (SEQ ID No 17, CFP-10), Rv3875 (SEQ ID No 18, ESAT-6), Rv3876 (SEQ ID No 19), Rv3877 (SEQ ID No 20), Rv3878 (SEQ ID No 21), and Rv3879 (SEQ ID No 22).

65. (New) A strain according to claim 1, wherein the strain has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), wherein the integrated DNA comprises at least one gene or fragment thereof selected from the group consisting of Rv3861 (SEQ ID No 4), Rv3862 (SEQ ID No 5), Rv3863 (SEQ ID No 6), Rv3864 (SEQ ID No 7), Rv3865 (SEQ ID No 8), Rv3866 (SEQ ID No 9), Rv3867 (SEQ ID No 10), Rv3868 (SEQ ID No 11), Rv3869 (SEQ ID No 12), Rv3870 (SEQ ID No 13), Rv3880 (SEQ ID No 23), Rv3881 (SEQ ID No 24), Rv3882 (SEQ ID No 25),

Rv3883 (SEQ ID No 26), Rv3884 (SEQ ID No 27), or Rv3885 (SEQ ID No 28) in combination with at least one gene or fragment thereof selected from the group consisting of Rv3871 (SEQ ID No 14), Rv3872 (SEQ ID No 15, mycobacterial PE), Rv3873 (SEQ ID No 16, PPE), Rv3874 (SEQ ID No 17, CFP-10), Rv3875 (SEQ ID No 18, ESAT-6), Rv3876 (SEQ ID No 19), Rv3877 (SEQ ID No 20), Rv3878 (SEQ ID No 21), and Rv3879 (SEQ ID No 22).

66. (New) A strain according to claim 60, wherein the coding sequence of the integrated gene is in frame with its natural promoter or with an exogenous promoter that directs high level of expression of said coding sequence.

67. (New) A strain according to claim 5, wherein the said integrated gene is mutated so as to maintain the improved immunogenicity while decreasing the virulence of the strain.

68. (New) A strain according to claim 66, wherein said strain only carries parts of the genes coding for ESAT-6 or CFP-10 in a mycobacterial expression vector under the control of an hsp60 promoter.

69. (New) A strain according to claim 66, wherein said strain carries at least one portion of the esat-6 gene that codes for immunogenic 20-mer peptides of ESAT-6 active as T-cell epitopes.

70. (New) A strain according to claim 67, wherein the esat-6 encoding gene is altered by directed mutagenesis in a way that most of the immunogenic peptides of ESAT-6 remain intact, but the biological functionality of ESAT-6 is lost.

71. (New) A strain according to claim 67, wherein the CFP-10 encoding gene is altered by directed mutagenesis in a way that most of the immunogenic peptides of CFP-10 remain intact, but the biological functionality of CFP-10 is lost.